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10/568,419	02/14/2006	Ian Smith	2538 US	7609

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GEORGE A. SEABY
SEABY & ASSOCIATES
250 CITY CENTRE AVNUE
OTTAWA, ON K1R6K7
CANADA

EXAMINER
SANG, HONG

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1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on <u>14 February 2006</u>.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) <u>1-5</u> is/are pending in the application.

    4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) <u>1-5</u> is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

    a)☐ All b)☐ Some * c)☐ None of:

      1.☐ Certified copies of the priority documents have been received.

      2.☐ Certified copies of the priority documents have been received in Application No. _____.

      3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

    * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application

6)☐ Other: _____.

DETAILED ACTION

RE: Smith et al.

1.   Claims 1-5 are pending and under examination.

Specification

2.   The first line of the specification should be updated if applicant desires priority

under 35 U.S.C. 1 19(e), 120, 121 and 365(c) based upon a previously filed application,

specific reference to the earlier filed application must be made in the instant application.

For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the

relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

This should appear as the first sentence of the specification following the title, preferably

as a separate paragraph unless it appears in an application data sheet. The status of

nonprovisional parent application (s) (whether patented or abandoned) should also be

included. If a parent application has become a patent, the expression "now Patent

No.___" should follow the filing date of the parent application. If a parent application has

become abandoned, the expression "now abandoned" should follow the filing date 6f

the parent application.

        For additional information, see United States Patent and Trademark Office OG

Notices: 1268 OG 89 (18 March 2003) "Benefit of Prior-Filed Application".

Appropriate correction is required.

Claim Rejections - 35 USC § 102

3.   The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that

form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4.   Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by

Craine (US2002/0076820A1, Pub. Date: 6/20/2002).

Craine teaches a method for determining whether blood in a stool sample came

from an upper gastrointestinal (GI) site or a lower gastrointestinal site comprising the

steps of: collecting a stool sample, placing the stool sample in a buffer to make a stool

sample suspension, obtaining the supernatant of the stool sample suspension,

subjecting the supernatant to a spectroscopy; determining a sample absorption spectra

of the stool sample; and determining whether blood in a stool sample came from an

upper gastrointestinal site or a lower gastrointestinal site based on analysis of the

sample absorption spectra (see claims 1, 5, 13 and 14), wherein the spectroscopy is a

Fourier transform infra-red spectroscopy (see claim 24). Craine teaches that the most

important application of testing for occult GI bleeding is to detect lower GI bleeding as a

screen for colorectal neoplasia (see paragraphs [0007] and [0018]). Craine teaches

that the normal level of blood loss is about 0.5µl of blood per 40mg stool, while a level of

about 7µl of blood per 40mg stool is considered to be positive occult bleed (see

paragraph [0038]). Craine teaches that the method further comprising a step of

classifying the type of gastrointestinal bleed based on a mathematical analysis of the

sample absorption spectra, wherein the mathematical analysis of the sample absorption

spectra can be accomplished by various algorithms, for example use of a trained

artificial neural network running on a computing device (see paragraph [0047], claims 9

and 17). While Craine does not specifically disclose comparing the spectra of patients

having intestinal bleeding with those of normal individuals, because the individuals to be

screened include both normal individuals and cancer patients, by detecting positive and

negative GI bleeding, Craine consequently teaches comparing the cancer to non-

cancerous individuals.

Claim Rejections - 35 USC § 103

5.   The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set
> forth in section 102 of this title, if the differences between the subject matter sought to be patented and
> the prior art are such that the subject matter as a whole would have been obvious at the time the
> invention was made to a person having ordinary skill in the art to which said subject matter pertains.
> Patentability shall not be negatived by the manner in which the invention was made.

6.   Claims 1, 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable

over Craine (US2002/0076820A1, Pub. Date: 6/20/2002) in view of Levin et al. (WO

02/12879A2, Pub. Date: 2/14/2002).

The teachings of Craine have been set forth above and as they apply to claims 1

and 4.

Craine does not teach the steps of selecting subregions from the spectra of stool

that are maximally discriminatory between non-cancerous and cancerous subjects;

repeatedly partitioning the data thus obtained into approximately equal sized random

training and test subsets; finding an optimal classifier for each random training subset; validating the accuracy of the optimal classifier on the random test subset; and determining the ultimate classifier as the weighted average of the classifier coefficients of a large number of individual component classifiers. However, these deficiencies are made up for in the teachings of Levin et al.

Levin et al. teach mathematical analysis of sample absorption spectra comprising the steps of selecting from the spectra resulting from the one-dimensional magnetic resonance spectroscopy maximally discriminatory subregions; repeatedly partitioning the data into approximately equal sized random training and test subsets; finding an optimal classifier for each random training subset and validating the accuracy of the optimal classifier on the random test subset; and determining the ultimate classifier as the weighted average of the classifier coefficients of a large number of individual component classifiers (see claim 5).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the mathematical analysis strategy of Levin to classify Craine's Infrared spectra. One would have been motivated to do so because Craine teaches classifying the type of gastrointestinal bleed based on a mathematical analysis of the sample absorption spectra, and Levin et al. teach their classification method provides excellent differentiation power. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to use the mathematical analysis strategy of Levin classify Craine's Infrared spectra because Levin teaches how to classify the absorption spectra using their mathematical algorithm.

7.   Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Argov et al. (J. Biomedical Optics, 2002, 7(2): 248-254), in view of Lapidus et al. (US

Patent No. 5,741,650, Date of Patent 4/21/1998), Stallings et al. (US/2003/0086869,

Pub. Date: 5/8/2003, effective filing date at least 6/5/2002), and Levin et al. (WO

02/12879A2, Pub. Date: 2/14/2002).

Argov et al. teach a method for detecting colon cancer, a method of

differentiating between adenomatous polyp and malignant colon cancer, a method of

classification of normal, polyp and malignant samples comprising detecting biological

markers such as phosphate content, RNA/DNA, carbohydrate in colon tissue of a

patient using Fourier-transform infrared spectroscopy and artificial neural network

(ANN) analysis (see abstract, pages 251-252). Argov et al. disclose that the tissue

samples were deparaffinized, dehydrated and analyzed by FT infrared spectroscopy

(see page 249)

Argov et al. do not teach the sample is a stool sample. Argov et al. do not teach

the stool sample is a saline suspension of stool sample. Argov et al. do not teach the

steps of selecting subregions from the spectra of stool that are maximally discriminatory

between non-cancerous and cancerous subjects; repeatedly partitioning the data thus

obtained into approximately equal sized random training and test subsets; finding an

optimal classifier for each random training subset; validating the accuracy of the optimal

classifier on the random test subset; and determining the ultimate classifier as the

weighted average of the classifier coefficients of a large number of individual

component classifiers. However, these deficiencies are made up for in the teachings of Lapidus, Stallings, and Levin et al.

Lapidus et al. teach a method for screening for the presence of a subpopulation of cancerous or precancerous cells in a stool sample (see abstract). Lapidus et al. teach that markers indicative of the presence of cancer, including cells, cellular debris, DNA, blood and carcinoembryonic antigen are shed onto the portion of the forming stool that contacts the cancerous tissue as the stool passes through the colon (see column 5, lines 14-18). Lapidus et al. teach a method of obtaining a representative sample of stool (see abstract). Lapidus et al. teach that once a cross-sectional stool sample is obtained, it may be homogenized by known methods to distribute cells and cellular debris throughout the sample, and the homogenate or an extract of the homogenate is analyzed by various assays to detect the presence of cells and/or cell debris (see column 6, lines 1-6). Lapidus et al. teach that the stool is homogenized in an appropriate buffer, such as phosphate buffered saline (see column 8, lines 5-8).

Stallings teaches that fecal homogenate can be directly analyzed by infrared spectroscopy (see paragraph [0017]).

Levin et al. teach that one dimensional protein NMR of human stool can be used in a non-invasive method of detecting the presence of colorectal cancer and/or clinically significant adenomas, wherein the spectrum of a patient's stool is compared with that of stool from non-cancerous subjects, observed differences in spectra being indicative of cancer and/or clinically significant adenomas (see abstract). Levin et al. teach mathematical analysis of sample absorption spectra comprising the steps of selecting

from the spectra resulting from the one-dimensional magnetic resonance spectroscopy maximally discriminatory subregions; repeatedly partitioning the data into approximately equal sized random training and test subsets; finding an optimal classifier for each random training subset and validating the accuracy of the optimal classifier on the random test subset; and determining the ultimate classifier as the weighted average of the classifier coefficients of a large number of individual component classifiers (see claim 5).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Argov to use stool sample (i.e. stool homogenate or supernatant of homogenate) instead of colon tissue for detecting colon adenoma polyp and/or colon caner in view of the teaching of Lapidus, Stallings, and Levin. One would have been motivated to do so because Lapidus et al. teach that the stool of the colon adenoma or cancer patients contains useful precancerous and/or cancerous markers, and Levin et al. have shown that the stool sample can be analyzed by NMR for classifying normal, colon adenoma and cancer. Moreover, unlike using tissue sample, the method of detecting colon adenoma and cancer using stool sample is simple and non-invasive. One of ordinary skill in the art would have a reasonable expectation of success to modify the method of Argov to use stool sample (i.e. stool homogenate or supernatant of homogenate) instead of colon tissue for detecting colon adenoma polyp and/or colon caner because Argov et al. teach a method of detecting colon adenoma and/or cancer using tissue sample by infrared spectroscopy, Lapidus and Levin both have shown that stool sample contains useful precancer and cancer

markers. Furthermore, Lapidus et al. teach how to obtain a representative stool sample, and Stallings teaches that the stool homogenate can be directly analyzed by infrared spectroscopy.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Argov to use the mathematical analysis strategy of Levin to classify Infrared spectra. One would have been motivated to do so because Levin et al. have shown that their classification method provides excellent differentiation power in stool analysis. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to modify the method of Argov to use the mathematical analysis strategy of Levin et al. to classify Infrared spectra because Levin teaches how to classify the absorption spectra using their mathematical algorithm.

Conclusion

8.   No claims are allowed.

9.   Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information

system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hong Sang, Ph.D.
Art Unit 1643
May 23, 2007

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER